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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
YOUNG, SHAWQUIA	
ART UNIT	**PAPER NUMBER**
1626	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/09/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/521,325	BONNERT ET AL.	
	Examiner	Art Unit	
	Shawquia Young	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,9-11 and 14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,9-11 and 14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/14/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-7, 9-11, and 14 are currently pending in the instant application. Claims 8, 12 and 13 were cancelled by preliminary amendment.

I. Priority

The instant application is a 371 of PCT/SE03/01216, filed on July 15, 2003, which claims benefit of Foreign Applications SWEDEN 0202241-6, filed on July 17, 2002 and SWEDEN 0203712-3, filed on December 13, 2002.

II. Information Disclosure Statement

The information disclosure statement (IDS) submitted on March 16, 2006 and August 7, 2006 have been considered by the examiner. See Applicant's copies of the 1449.4

III. Rejection(s)

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

(1) Claims 1-7, 9-11 and 14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The following terms of Claim

1 are not defined in the specification so as to know the structures of the compounds that are included and/or excluded by the term: "heteroaryl" when defining variables R^1 and R^5-R^{15}. Therefore, the specification lacks adequate support for Claim 1.

Applicant may overcome this rejection by pointing out where in the specification the terms are defined or by deleting the undefined terms.

(2) Claims 9 and10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As stated in the MPEP 2164.01 (a), "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue".

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have need described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,

5. the presence or absence of working examples,

6. the breadth of the claims,

7. the quantity of experimentation needed, and

8. the level of the skill in the art.

In the instant case,

The nature of the invention

The nature of the invention of claims 9 and 10 is a method of treating a disease mediated by prostaglandin D2, which comprises administering to a patient a therapeutically effective amount of a compound of formula (I) or a pharmaceutically acceptable salt as defined in claim1.

The state of the prior art and the predictability or lack thereof in the art

The state of the prior art is that the pharmacological art involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific disease by what mechanism). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F. 2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is

the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art would recognize that in regards to therapeutic effects of diseases mediated by prostaglandin D2 would make a difference.

Applicants are claiming a method of treating a disease mediated by prostaglandin in a patient. Further, applicants fail to identify diseases or disorders mediated by prostaglandin D2 that can be treated by using the claimed invention. According to applicants' specification, the above diseases include asthma, rhinitis, Alzheimer's disease, stroke, etc (See pages 16-17).

Applicants' claims are therefore drawn to the treatment of Alzheimer's disease. It is the state of the art that there is no known cure or prevention for Alzheimer's disease and that there are only four medications available in the United States available to temporarily slow the early stages of Alzheimer's disease. The current drugs for the treatment of Alzheimer disease, Aricept, Exelon, Reminyl and Cognex, treat early stages of Alzheimer's disease by delaying the breakdown of acetylcholine. Memantine, which blocks excess amounts of glutamate treats late stage Alzheimer's disease. (<URL:http://www.cnn.com/2003/HEALTH/conditions/09/24/alzheimers.drug.ap/index.html>.)

In addition, Layzer, Cecil Textbook of Medicine (article enclosed), states that "some degenerative diseases are difficult to classify because they involve multiple anatomic locations" (see page 2050). Alzheimer's disease has traditionally been very difficult or impossible to prevent or even to treat effectively with chemotherapeutic

agents (*See* e.g., the Cecil Textbood of Medicine, 20th edition (1996), Vol. 2, page 1994).

Applicants are also claiming a treatment of stroke. Stroke represents on of the most intractable medical challenges. Stroke is estimated to cause about 15% of deaths. Even those who survive normally suffer from persistent damage, including motor and speech disturbances and/or convulsions. Despite a tremendous effort to resolve these problems, cerebrovascular therapy as so far been limited to trying to prevent further damage in areas on the margins of the ischemic focus, thus trying to maintain adequate perfusion in remaining intact areas, and thereby limit progressive infarction. This is generally done surgically. Standard pharmaceutical treatment, such as antiarrhythmics and antithrombotics don't get at the cause of the stroke or the damage caused, but are mostly done to insure adequate cardiac functioning.

Hence, in the absence of a showing of correlation between all the diseases encompassed by the claims as capable of treatment by activating the CRTh2 receptor, one of skill in the art is unable to fully predict possible results from the administration of the compound of the claims due to the unpredictability of the role of binding at CRTh2 receptors and, for example, since it is no known cure for Alzheimer's disease and treatment protocols for Alzheimer's disease depend on the stage of the disease.

The amount of direction present and the presence or absence of working examples

The only direction or guidance present in the instant specification is the listing of various diseases applicant considers as treatable by the claimed invention found on pages 16-17. There are no working examples present for the treatment of any disease or disorder by activating CRTh2 receptor.

Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved." See In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

The breadth of the claims

The breadth of the claims is the treatment of diseases such as asthma, rhinitis, Alzheimer's disease, stroke, etc. Furthermore, the instant claims cover "diseases" that are known to exist and those that may be discovered in the future, for which there is no enablement provided.

The diseases encompassed by the instant claims include, for example, Alzheimer's disease and stroke, some of which have been proven to be extremely difficult to treat. Further, there is no reasonable basis for assuming that the myriad of compounds embraced by the claims will all share the same physiological properties since they are so structurally dissimilar as to be chemically non-equivalent and there is no basis in the prior art for assuming the same.

The quantity of experimentation needed

The quantity of experimentation needed is undue experimentation. One of skill in the art would need to determine what diseases out of all diseases would be benefited by

the activation of CRTh2 receptors and would furthermore then have to determine which of the claimed compounds in the instant invention would provide treatment of which disease, if any.

The level of the skill in the art

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by *in vitro* or *in vivo* screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

The specification fails to provide sufficient support of the broad use of the claimed compounds of the invention in a method of treating a disease mediated by prostaglandin D2. As a result necessitating one of skill to perform an exhaustive search for which diseases can be treated by what compounds of the invention in order to practice the claimed invention.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to

engage in undue experimentation to test which diseases can be treated by the compound encompassed in the instant claims, with no assurance of success.

This rejection can be overcome, for example, by deleting the method claims.

(3) Claim 14 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The "protected derivatives" of the compounds of formula (II) or (III) are not defined in the specification so as to know the structures of the compounds that are included and/or excluded by the term. Therefore, the specification lacks adequate support for Claims 14.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

(4) Claim 4 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite and unclear. Claim 4 mentions " a compound according to claim 1 in which the substituent(s) is/are in the 4- and/or 5-position", however there are various variables that can have substituents mentioned in claim 1. It is unclear which substituents on which portion of the structure are in the 4- and/or 5-position. Appropriate correction is required.

(5) Claim 14 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant

regards as the invention. Claim 14 is indefinite for the reasons set forth above under 35 U.S.C. 112, first paragraph. Claim 14 involves the process steps: (a) oxidation of a compound of formula (II) or are protected derivatives thereof or (b) reaction of a compound of formula (III) or are protected derivatives thereof. However, the "protected derivatives" of the compounds of Claims 14 is not defined in the claim so as to know the metes and bounds of the claims. Therefore, the claim is indefinite.

Further, Claim 14 is unclear because it contains the phrase "comprises reaction of a compound of formula (II)". The Examiner interprets the claim as being drawn to a process for preparing a compound of formula (I) which comprises reaction of a compound of formula (II) wherein the reaction of a compound of formula (II) can comprise of step (a) oxidation of a compound of formula (II) or step (b) reaction of a compound of formula (III). However, it seems that the claim can also be interpreted as a compound of formula (I) can be prepared by either step (a) or step (b). It is suggested that Applicants delete the phrase "reaction of a compound of formula II" in claim 14 to clarify the claimed subject matter.

(6) 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 11 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The phrase "Use of a compound of formula (I) are written in improper format because a "use" can only be properly claimed as a process or method. It is suggested that applicant amend the claims by rewriting the claims as a

process or method, i.e. "a method of manufacturing a medicament ..."

IV. *Objections*

Specification

The disclosure is objected to because of the following informalities: a hydrogen atom is missing on the carboxylic acid in Examples 12, 17, 18, 20-23 and 25-29.

Appropriate correction is required.

Claim Objections

Claims 1-7, 9-11 and 14 are objected to because of the following informalities: claim 1 contains the misspelled term "heteraryl". The correct spelling of the term should be "heteroaryl". In Claim 11, the phrase "of a compound" is mentioned twice. It is suggested that Applicant deletes one of the phrases "of a compound". Appropriate correction is required.

V. Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shawquia Young whose telephone number is 571-272-9043. The examiner can normally be reached on 8:00 AM-4:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on 571-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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